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L3 ANSWER 1 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. DUPLICATE
1

2001:517733 Document No.: PREV200100517733. Plasmid-based **vaccine**
for treating atherosclerosis. Thomas, Lawrence J. (1). (1) Easton, MA
USA.

ASSIGNEE: AVANT Immunotherapeutics, Inc.. Patent Info.: US 6284533
September 04, 2001. Official Gazette of the United States Patent and
Trademark Office Patents, (Sep. 4, 2001) Vol. 1250, No. 1, pp. No
Pagination. e-file. ISSN: 0098-1133. Language: English.

AB A plasmid-based **vaccine** is provided herein based on the
combination of DNA segments coding for one or more B cell epitopes of
cholesteryl ester transfer protein (CETP) and one or more broad
range helper T cell epitopes. Administration of the plasmids as a
vaccine to a vertebrate subject provides an immune response to the
subject's endogenous CETP and modulation of CETP
activity, leading to prevention or reversal of various manifestations of
heart disease. The **vaccines** provide an advantageous strategy for
the prevention or treatment of atherosclerosis.

L3 ANSWER 2 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC. DUPLICATE
2

2001:298985 Document No.: PREV200100298985. An extended toxicologic
evaluation

of an immunoneutralizing **vaccine** to produce anti-CETP
antibodies for the prevention/treatment of atherosclerosis. Thomas,
Lawrence J. (1); Picard, Michele D. (1); Miller, David P. (1); Emmett,

Constance D. (1); Scesney, Susanne M. (1); Pisano, Milissa L. (1); Adari, Hedy (1); Hammond, Russell A. (1); Marsh, Henry C. (1); Rittershaus, Charles W. (1); Pettey, Carolyn L. (1). (1) AVANT Immunotherapeutics, 119 Fourth Ave., Needham, MA, 02494 USA. FASEB Journal, (March 7, 2001) Vol. 15, No. 4, pp. A566. print. Meeting Info.: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001 ISSN: 0892-6638. Language: English. Summary Language: English.

AB A toxicology study was conducted with an immunoneutralizing **vaccine** designed to elicit antibodies that would bind to and block the function of cholesteryl ester transfer protein (**CETP**), in order to prevent atherosclerosis. The **vaccine** consisted of a dimer of a 31 a.a. synthetic chimeric peptide containing an N-terminal cysteine, a T cell epitope (residues 830-843 of tetanus toxin), and a B cell epitope (residues 461-476 of human **CETP**), formulated with an alum adjuvant. In this study NZW rabbits were immunized with either 0 mg (4 males and 4 females), 0.1 mg (2 males and 2 females), 0.25 mg (4 males and 4 females) or 1.0 mg (4 males and 4 females) of the **vaccine** on days 1, 29 and 57. On day 197 (at a relative antibody minimum) half of the animals from groups 1, 3 and 4 were sacrificed. The remaining animals were reboosted and euthanized on day 211, at an expected

antibody maximum. Blood samples were taken periodically throughout the study and were assessed for hematology, clinical chemistry, and antibody titers. All rabbits in the non-control groups developed anti-rabbit **CETP** antibody titers, thus validating the immunogenicity of the **vaccine**. In all other measurements the vaccinated groups were indistinguishable from the control group. All animals were monitored for clinical abnormalities throughout the study, and at necropsy, gross pathology was assessed, selected organs were weighed, and samples of 44 tissues were taken for histopathology. By all the above parameters, no significant test article-related pathology was observed. This study demonstrated the administration of this **CETP** immunoneutralizing **vaccine** produced specific self-reactive antibody titers but no detectable test article-related pathology.

L3 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2002 ACS

2002:4125 An immunotherapeutic approach for the treatment of low plasma HDL-Cholesterol. Ryan, Una S.; Rittershaus, Charles W. (AVANT Immunotherapeutics, Inc., Needham, MA, 02494-2725, USA). NATO Science Series, Series I: Life and Behavioural Sciences, 330 (Vascular Endothelium), 26-33 (English) 2001. CODEN: NSSC9. ISSN: 1566-7693. Publisher: IOS Press.

AB One determinant of plasma HDL-Cholesterol concn. is cholesteryl ester transfer protein (**CETP**) activity. Inhibition of **CETP** activity increases plasma HDL-C, thus providing a potential therapeutic target for the treatment of atherosclerosis. Using a **vaccine** approach, we immunized New Zealand White rabbits with a peptide contg. a region of **CETP** known to be required for neutral lipid transfer function. **CETP**-vaccinated rabbits had significantly reduced plasma **CETP** activity and an altered lipoprotein profile compared with control rabbits. In a cholesterol-fed rabbit model of atherosclerosis, the fraction of plasma cholesterol in HDL was 42% higher, and the fraction of plasma cholesterol in LDL was 24% lower in the **CETP**-vaccinated group compared with the control-vaccinated group. Moreover, the percentage of the aorta surface exhibiting atherosclerotic lesion was 39.6% smaller in the **CETP**-vaccinated rabbits compared with controls. The data reported here demonstrate that **CETP** activity can be reduced in vivo by vaccination with a peptide derived from **CETP**, and support the concept that inhibition of **CETP** activity in vivo can be anti-atherogenic. Currently, this **vaccine** is in clin. trials.

2000482102 Document Number: 20436374. PubMed ID: 10978256.

Vaccine-induced antibodies inhibit CETP activity in vivo and reduce aortic lesions in a rabbit model of atherosclerosis. Rittershaus C W; Miller D P; Thomas L J; Picard M D; Honan C M; Emmett C D; Pettey C L; Adari H; Hammond R A; Beattie D T; Callow A D; Marsh H C; Ryan U S. (AVANT Immunotherapeutics, Inc, Needham, MA 02494, USA.. crittershaus@avantimmune.com) . ARTERIOSCLEROSIS, THROMBOSIS, AND

VASCULAR

BIOLOGY, (2000 Sep) 20 (9) 2106-12. Journal code: B89; 9505803. ISSN: 1524-4636. Pub. country: United States. Language: English.

AB Using a vaccine approach, we immunized New Zealand White rabbits with a peptide containing a region of cholesteryl ester transfer protein

(

CETP) known to be required for neutral lipid transfer function. These rabbits had significantly reduced plasma CETP activity and an altered lipoprotein profile. In a cholesterol-fed rabbit model of atherosclerosis, the fraction of plasma cholesterol in HDL was 42% higher and the fraction of plasma cholesterol in LDL was 24% lower in the CETP-vaccinated group than in the control-vaccinated group. Moreover, the percentage of the aorta surface exhibiting atherosclerotic lesion was 39.6% smaller in the CETP-vaccinated rabbits than in controls. The data reported here demonstrate that CETP activity can be reduced in vivo by vaccination with a peptide derived from CETP and support the concept that inhibition of CETP activity in vivo can be antiatherogenic. In addition, these studies suggest that vaccination against a self-antigen is a viable therapeutic strategy for disease management.

L3 ANSWER 5 OF 15 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

2000421271 EMBASE Genetic polymorphisms and activity of cholesterol ester transfer protein (CETP): Should we be measuring them?. Ordovas J.M.. J.M. Ordovas, Lipid Metabolism Laboratory, Jean Mayer USDA Hum. Nutr. Res. Ctr., Tufts University, Boston, MA, United States. Ordovas@hnrc.tufts.edu. Clinical Chemistry and Laboratory Medicine 38/10 (945-949) 2000.

Refs: 51.

ISSN: 1434-6621. CODEN: CCLMFW. Pub. Country: Germany. Language: English. Summary Language: English.

AB Cholesteryl ester transfer protein (CETP) is a plasma glycoprotein that mediates the transfer of cholesteryl ester from high density lipoproteins (HDL) to triglyceride-rich lipoproteins in exchange for triglycerides. Several approaches are currently being used in research

laboratories to measure its activity and/or mass. However, these assays are not standardized and it is not possible to compare data from different

laboratories. Also, we lack enough information to assess the value of this

variable as a coronary heart disease (CHD) predictor. Several genetic variants at CETP locus have been identified and they have been generally associated with increased HDL- cholesterol concentrations. However, there is no consensus about the association of this CETP-related increase in HDL-cholesterol and protection against CHD. Nevertheless, the most recent evidence from the common CETP

-Taql-B polymorphism shows that the lower CETP activity associated with the presence of this polymorphism decreases CHD risk in men. Based on this and previous evidence, there has been an interest in the development of CETP inhibitors as a tool to increase HDL-cholesterol, thus reducing CHD risk. However, it should be noted that the evidence about the cardioprotective role of these drugs is not yet available.

2000:559012 The Genuine Article (R) Number: 313NH. Toxicologic evaluation of an immunoneutralizing **vaccine** to produce anti-**CETP** antibodies for the prevention/treatment of atherosclerosis.. Thomas L J (Reprint); Picard M D; Miller D P; Emmett C D; Scesney S M; Adari H; Hammond R A; Levin J L; Ryan U S; Marsh H C; Pettey C L; Rittershaus C W.

AVANT IMMUNOTHERAPEUT INC, NEEDHAM, MA 02494. FASEB JOURNAL (11 MAY 2000)

Vol. 14, No. 8, pp. 262-262. Publisher: FEDERATION AMER SOC EXP BIOL.

9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998. ISSN: 0892-6638. Pub. country: USA. Language: English.

1999:282118 Document No. 130:310673 Xenogeneic cholestryl ester transfer protein (**CETP**) for modulation of **CETP** activity in treatment of atherosclerosis. Rittershaus, Charles W.; Thomas, Lawrence J. (Avant Immunotherapeutics, Inc., USA). PCT Int. Appl. WO 9920302 A1 19990429, 62 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US22145 19981020. PRIORITY: US 1997-954643 19971020.

AB Methods for modulating cholestryl ester transfer protein (**CETP**) activity and the plasma levels of lipoproteins involved in heart disease involve administration of a non-endogenous **CETP** or a plasmid-based **vaccine** for expression of such non-endogenous **CETP** to elicit prodn. in a mammal of antibodies that recognize (bind to) the mammal's native (endogenous) **CETP**.

1999:223038 Document No. 130:250711 Vector **vaccines** against cholesterol ester transfer protein for the treatment of atherosclerosis. Needleman, Philip; Glenn, Kevin (Monsanto Company, USA). PCT Int. Appl. WO 9915655 A1 19990401, 99 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ,

BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US19366 19980917.

PRIORITY: US 1997-934367 19970919.

AB Expression vectors for manuf. of antigenic fragments of cholestryl ester transfer protein (**CETP**) that can be used to inactivate the protein are described. The protein plays a key role in the transfer of cholesterol from HDL to LDL and VLDL and inhibition of **CETP** synthesis can be used to prevent LDL and VLDL formation in the prophylaxis

of atherosclerosis. Immunogens, inocula, DNA segments, and recombinant DNA mol. vectors useful for carrying out the invention are also disclosed.

The use of antigenic fragments of rabbit **CETP** to raise autoantibodies in rabbits is demonstrated. Antibodies to three such peptides cross-reacted with human **CETP**. Rabbits vaccinated with these antigens showed a .apprx.10% increase in serum HDL. Antigens were manufd. as fusion proteins with hepatitis B core antigens in Escherichia coli, in a baculovirus system, and in mammalian cell culture.

L3 ANSWER 9 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
4

1999:282999 Document No.: PREV199900282999. A **vaccine** to produce anti-cholesterol ester transfer protein (**CETP**) antibodies for the prevention/treatment of atherosclerosis. Thomas, L. J. (1); Picard, M. D. (1); Miller, D. P. (1); Honan, C. M. (1); Adari, H. (1); Emmett, C. D. (1); Marsh, H. C. (1); Ryan, U. S. (1); Pettey, C. L. (1); Rittershaus, C. W. (1). Avant Immunotherapeutics, Inc., Needham, MA, 02494 USA. FASEB Journal, (March 15, 1999) Vol. 13, No. 5 PART 2, pp. A693. Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 99 Washington, D.C., USA April 17-21, 1999 Federation of American Societies for Experimental Biology. ISSN: 0892-6638. Language: English.

L3 ANSWER 10 OF 15 SCISEARCH COPYRIGHT 2002 ISI (R)

1998:762763 The Genuine Article (R) Number: 121HC. Use of xenogeneic cholesterol ester transfer protein (**CETP**) in a plasmid-based **vaccine** to produce anti-**CETP** autoantibodies for the prevention/treatment of atherosclerosis.. Thomas L J (Reprint); Adari H; Picard M D; Honan C M; Miller D P; Rittershaus C W; Pettey C L. T CELL SCI INC, NEEDHAM, MA. FASEB JOURNAL (17 MAR 1998) Vol. 12, No. 4, Part 1, Supp. [S], pp. 1805-1805. Publisher: FEDERATION AMER SOC EXP BIOL. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998. ISSN: 0892-6638. Pub. country: USA. Language: English.

L3 ANSWER 11 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

1998:200178 Document No.: PREV199800200178. Use of xenogeneic cholesterol ester transfer protein (**CETP**) in a plasmid-based **vaccine** to produce anti-**CETP** autoantibodies for the prevention/treatment of atherosclerosis. Thomas, L. J.; Adari, H.; Picard, M. D.; Honan, C. M.;

Miller, D. P.; Rittershaus, C. W.; Pettey, C. L.. T Cell Sciences Inc., Needham, MA USA. FASEB Journal, (March 17, 1998) Vol. 12, No. 4, pp.

A310. Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 98, Part 1 San Francisco, California, USA April 18-22, 1998 Federation of American Societies for Experimental Biology. ISSN: 0892-6638. Language: English.

L3 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2002 ACS

1997:740308 Document No. 128:10315 Plasmid-based **vaccine** for treating atherosclerosis. Thomas, Lawrence J. (T Cell Sciences, Inc., USA; Thomas, Lawrence J.). PCT Int. Appl. WO 9741227 A1 19971106, 66 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ,

DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US7294 19970501.

PRIORITY: US 1996-640713 19960501; US 1997-802967 19970221.

AB A plasmid-based **vaccine** is provided that is based on the combination of DNA segments coding for one or more B cell epitopes of **CETP** and one or more broad range helper T cell epitopes. Administration of the plasmids as a **vaccine** to a vertebrate subject provides an immune response to the subject's endogenous **CETP** and modulation of **CETP** activity, leading to prevention or reversal of various manifestations of heart disease. The **vaccines** provide an advantageous strategy for the prevention or treatment of atherosclerosis.

L3 ANSWER 13 OF 15 SCISEARCH COPYRIGHT 2002 ISI (R)
97:166073 The Genuine Article (R) Number: WH142. A plasmid-based
vaccine to elicit autoantibodies to cholesteryl ester transfer
protein (CETP) for the prevention/treatment of atherosclerosis..
Thomas L J (Reprint); Picard M D; Stewart S E; WAite B C D; Lin A Y;
Rittershaus C W; Pettey C L. T CELL SCI INC, NEEDHAM, MA. JOURNAL OF
ALLERGY AND CLINICAL IMMUNOLOGY (JAN 1997) Vol. 99, No. 1, Part 2, Supp.
[S], pp. 754-754. Publisher: MOSBY-YEAR BOOK INC. 11830 WESTLINE
INDUSTRIAL DR, ST LOUIS, MO 63146-3318. ISSN: 0091-6749. Pub. country:
USA

. Language: English.

L3 ANSWER 14 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
1997:144273 Document No.: PREV199799443476. A plasmid-based vaccine
to elicit autoantibodies to cholesteryl ester transfer protein (CETP)
for the prevention/treatment of atherosclerosis. Thomas, L.
J.; Picard, M. D.; Stewart, S. E.; Waite, B. C. D.; Lin, A. Y.;
Rittershaus, C. W.; Pettey, C. L.. T Cell Sci. Inc., Needham, MA USA.
Journal of Allergy and Clinical Immunology, (1997) Vol. 99, No. 1 PART 2,
pp. S187. Meeting Info.: Joint Meeting of the American Academy of
Allergy,
Asthma and Immunology, the American Association of Immunologists and the
Clinical Immunology Society San Francisco, California, USA February
21-26,
1997 ISSN: 0091-6749. Language: English.

L3 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2002 ACS
1997:12606 Document No. 126:46315 Modulation of cholesteryl ester transfer
protein (CETP) activity. Rittershaus, Charles W.; Thomas,
Lawrence J. (T Cell Sciences, Inc., USA; Rittershaus, Charles W.; Thomas,
Lawrence J.). PCT Int. Appl. WO 9634888 A1 19961107, 81 pp. DESIGNATED
STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK,
EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV,
MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK; RW:
AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE,
IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN:
PIXXD2. APPLICATION: WO 1996-US6147 19960501. PRIORITY: US 1995-432483
19950501.

AB This invention relates to peptides comprising a helper T cell epitope
portion and a B cell epitope portion for eliciting an immune response
against endogenous cholesteryl ester transfer protein (CETP)
activity, to prevent or treat cardiovascular disease, such as
atherosclerosis. The T helper T cell epitope may be derived from an
antigenic peptide selected from the group consisting tetanus toxoid,
diphtheria toxoid, pertussis vaccine, Bacille Calmette-Guerin,
polio vaccine, measles vaccine, mumps vaccine
, rubella vaccine, purified protein deriv. of tuberculin,
keyhole limpet hemocyanin, hsp70 and combination thereof.

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